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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,941	10/21/2003	Francine Denizeau	01023-0012	3312

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ROBIC
CENTRE CDP CAPITAL
1001 VICTORIA SQUARE
BLOC E - 8TH FLOOR
MONTREAL, QC H2Z2B7
CANADA

EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/688,941	DENIZEAU ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1 – 12 in the reply filed on March 13, 2006 is acknowledged.

Claims 13 – 20 are canceled. Claims 1 – 12 have been considered on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is drawn to a biocompatible support however is rendered vague and indefinite for reciting "it" in line 1, because it is unclear to what "it" refers.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1 – 5 and 8 – 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ingber et al (US 6309635 B1).

Applicant claims a biocompatible support structure comprising a biocompatible, nonbiodegradeable polymeric material wherein the polymeric material consists of a crosslinked PVA derivatized with alkylamino groups, and wherein when saturated in a suitable aqueous medium, the support forms a porous 3D, sponge like scaffold with pores that are distributed such that at least 0.1ml/min^-1cm^-2 of an aqueous solution circulates through the support. The pores are distributed such that a flow of at least 0.5 ml/min^-1cm^-2, or 1 – 15 solution may circulate; the pores have a diameter of about 100 – 1000 um; the structure has about 20 – 50 pores/cm^2. The support further comprises a polymer selected from PEG, agarose, starch, alginate and chitosan; or further comprises a bioactive molecule selected from extracellular biocompatible support structure proteins, growth factors, hormones, signaling molecules, peptide binding motifs, carbohydrates and carbohydrate derivatives. The cells are mammalian, specifically

human; more specifically are hepatocytes, cardiomyocytes, fibroblasts, osteoblasts, cancer cells, monoclonal cells, kidney cells or pancreatic cells.

Ingber teaches a biocompatible, biodegradable or non-biodegradable porous polymer scaffolding matrix with pore sizes of 100 – 300 microns, wherein the polymeric material is a PVA sponge (abstract, col.3 line 48-57). Biologically active compounds are added to the matrix (col.3 line64-col.4 line 2) and hepatocytes are added to and grown on the matrix (col.4 line 3-15). The preferred PVA is derivatized with alkyl groups (col.5 line 15-22) and polymers such as agarose and other materials known in the art are added to enhance cell attachment (col.5 line 33-39). The support can be used with many different cell types, such as pancreatic cells, depending on the application (col.6 line 50-60).

Ingber does not teach the support wherein the pores are dimensioned such that the claimed flow of an aqueous solution is achieved, the amount of pores, or wherein the cells are human. However, the pore dimensions and distributions are recognized result effective variables. Thus, at the time of the claimed invention, it would have been well within the purview of a person of ordinary skill in the art to optimize such variables as a matter of routine experimentation. Moreover, at the time the claimed invention was made, one of ordinary skill in the art would have been motivated by routine practice to optimize the pore dimension and/or distribution in the scaffold of Ingber with a reasonable expectation for successfully obtaining an effective biocompatible support structure. Regarding the use of human cells, Ingber demonstrates the effective supports in mice. A person of ordinary skill in the art would understand that such examples are meant to exemplify the effectiveness in a human subject, particularly since the claims are to treating a patient. Thus, at the time of the claimed invention,

it would have been obvious to one of ordinary skill in the art to use human cells in the biocompatible support while following the teachings of Ingber.

7. Claims 1 – 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ingber in view of Saavedra et al. (J Biomed Mater Res A, 2003).

Applicant claims a biocompatible support structure comprising a biocompatible, nonbiodegradeable polymeric material wherein the polymeric material consists of a crosslinked PVA derivatized with alkylamino groups, and wherein when saturated in a suitable aqueous medium, the support forms a porous 3D, sponge like scaffold with pores that are distributed such that at least 0.1ml/min^-1cm^-2 of an aqueous solution circulates through the support. The pores are distributed such that a flow of at least 0.5 ml/min^-1cm^-2, or 1 – 15 solution may circulate; the pores have a diameter of about 100 – 1000 um; the structure has about 20 – 50 pores/cm^2; the the PVA is derivatized by reacting the hydroxyl functions with haloalkyl amine selected from 2-chloroethylamine hydrochloride, chloropropyl amine, bromoethylamine and iodoethylamine. The support further comprises a polymer selected from PEG, agarose, starch, alginate and chitosan; or further comprises a bioactive molecule selected from extracellular biocompatible support structure proteins, growth factors, hormones, signaling molecules, peptide binding motifs, carbohydrates and carbohydrate derivatives. The cells are mammalian, specifically human; more specifically are hepatocytes, cardiomyocytes, fibroblasts, osteoblasts, cancer cells, monoclonal cells, kidney cells or pancreatic cells.

Ingber teaches a biocompatible, biodegradable or non-biodegradable porous polymer scaffolding matrix with pore sizes of 100 – 300 microns, wherein the polymeric material is a

PVA sponge (abstract, col.3 line 48-57). Biologically active compounds are added to the matrix (col.3 line64-col.4 line 2) and hepatocytes are added to and grown on the matrix (col.4 line 3-15). The preferred PVA is derivatized with alkyl groups (col.5 line 15-22) and polymers such as agarose and other materials known in the art are added to enhance cell attachment (col.5 line 33-39). The support can be used with many different cell types, such as pancreatic cells, depending on the application (col.6 line 50-60).

Ingber does not teach the support wherein the pores are dimensioned such that the claimed flow of an aqueous solution is achieved, the amount of pores, or wherein the cells are human. However, the pore dimensions and distributions are recognized result effective variables. Thus, at the time of the claimed invention, it would have been well within the purview of a person of ordinary skill in the art to optimize such variables as a matter of routine experimentation. Moreover, at the time the claimed invention was made, one of ordinary skill in the art would have been motivated by routine practice to optimize the pore dimension and/or distribution in the scaffold of Ingber with a reasonable expectation for successfully obtaining an effective biocompatible support structure. Regarding the use of human cells, Ingber demonstrates the effective supports in mice. A person of ordinary skill in the art would understand that such examples are meant to exemplify the effectiveness in a human subject, particularly since the claims are to treating a patient. Thus, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use human cells in the biocompatible support while following the teachings of Ingber.

Ingber does not teach the support wherein the PVA is derivatized with the claimed alkyl amines. However, Ingber does teach the PVA is derivatized with alkyl amines. Saavedra

teaches a PVA porous sponge derivatized with alkylamino groups wherein hepatocytes are seeded onto the structure (abstract). Specifically, the PVA is derivatized with 2-chloroethylamine hydrochloride, by methods described in 1985 (p.563, materials and methods). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Ingber and Saavedra to derivatize the PVA sponge with 2-chloroethylamine hydrochloride because it was a recognized product in cell support structures, as evidenced by Saavedra. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Ingber and Saavedra to derivatize the PVA of Ingber with 2-chloroethylamine hydrochloride, with a reasonable expectation for successfully obtaining an effective biocompatible support.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 571-272-0915. The examiner can normally be reached on M-F 7:00 - 2:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 14, 2006
AU 1651

RUTH A. DAVIS
PATENT EXAMINER